Refine Search

Search Results -

Terms	Documents
L1 and (multivesicular)	3

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L3

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Friday, February 17, 2006 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L3	L1 and (multivesicular)	3	L3
L2	(dna or rna or nucle$) adj5 (polycation or polylysine) adj10 liposome	38	L2
L1	(dna or rna or nucle$) adj5 (polycation or polylysine)	943	L1

END OF SEARCH HISTORY

L2: Entry 28 of 38 File: USPT Dec 28, 1999

DOCUMENT-IDENTIFIER: US 6008202 A
** See image for Certificate of Correction **
TITLE: Stable lipid-comprising drug delivery complexes and methods for their production

Detailed Description Text (6):
When a drug/lipid/polycation complex having a net positive charge and/or a positively charged surface is to be produced, the inclusion of the polycation reduces the amount of lipid which must be mixed with drug to the extent that the positive charge from the lipid may be less than the negative charge from the drug. This reduction in the amount of lipid reduces the toxicity of the polycation-containing formulations. Mole amounts of cationic liposomes to be used in formulating nucleic acid/lipid/polycation complexes may range from about 0.1 nmol to about 200 nmol lipid per 1 .mu.g nucleic acid, more preferably from about 1 to about 25 nmoles lipid per 1 .mu.g nucleic acid depending on the positive charge content of the cationic liposomes. It is to be generally understood that in producing the nucleic acid/lipid and nucleic acid/lipid/polycation complexes of the present invention, the mole amount of liposomes required to produce these complexes will increase as the concentration of nucleic acid mixed with the liposomes is increased.

Detailed Description Text (17):
In a preferred embodiment, the nucleic acid/lipid and nucleic acid/lipid/polycation complexes are produced by slowly adding nucleic acid to the solution of liposome or liposome plus polycation and mixing with a stirring bar where the mixing is allowed to proceed second after addition of DNA. Alternatively, the liposome or liposome/polycation mix can be added into a single chamber from a first inlet at the same time the nucleic acid is added to the chamber through a second inlet. The components are then simultaneously mixed by mechanical means in a common chamber. The complexes may also be produced by first mixing the nucleic acid with the polycation and then adding the liposome suspension.

Detailed Description Text (34):
The transfection activity of a polycationic polypeptide/DNA/lipid complex of the invention in CHO cells, is preferably equal to or greater than the transfection activity of a poly-L-lysine/DNA/lipid complex in CHO cells when each polycation is complexed with the same cationic liposome and plasmid construct containing a reporter gene where reporter genes include, but are not limited to, the chloramphenicol acetyl transferase gene, the luciferase gene, the .beta.-galactosidase gene and the human growth hormone gene, the alkaline phosphatase gene and a green fluorescent protein gene.

Detailed Description Text (35):
In producing nucleic acid/lipid/polycation complexes of the present invention, the ratio of polycation to nucleic acid is kept fixed while varying the amount of liposome. However, those of skill in the art would recognize that the ratio of polycation to nucleic acid will be affected by the charge density of the liposome to be mixed with the nucleic acid and polycation. For example, if the charge density of liposomes is decreased as a result of changes in the lipid composition of the liposome (eg decreasing the ratio of cationic lipid: neutral lipid in the

liposome), the amount of polycation to be mixed with nucleic acid and liposome may be increased to compensate for the decrease in positive charge contributed by the liposomes. However, when polycation is utilized, it is preferred to use subsaturating amounts of polycation (i.e., amounts which will not saturate all the negative charge of the nucleic acid) in order to allow the cationic lipids to complex with the nucleic acid. Thus, in a preferred embodiment of the invention, a positive charge excess of lipid to nucleic acid is used even when polycation is mixed with lipid and nucleic acid. Amounts of polycation which may be mixed with 1 .mu.g of nucleic acid and varying amounts of cationic liposomes in the present invention range from about 0.01 .mu.g to about 100 .mu.g of polycation per .mu.g of nucleic acid, preferably from about 0.1 .mu.g to about 10 .mu.g of polycation per .mu.g of nucleic acid.

Detailed Description Text (36):
Where purification of nucleic acid/lipid and nucleic acid/lipid/polycation complexes from excess free DNA, free liposomes and free polycation is desired, purification may be accomplished by centrifugation through a sucrose density gradient or other media which is suitable to form a density gradient. However, it is understood that other methods of purification such as chromatography, filtration, phase partition, precipitation or absorption may also be utilized. In a preferred method, purification via centrifugation through a sucrose density gradient is utilized. The sucrose gradient may range from about 0% sucrose to about 60% sucrose, preferably from about 5% sucrose to about 30% sucrose. The buffer in which the sucrose gradient is made can be any aqueous buffer suitable for storage of the fraction containing the complexes and preferably, a buffer suitable for administration of the complex to cells and tissues. A preferred buffer is pH 7.0-8.0 Hepes.

Previous Doc Next Doc Go to Doc#

First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

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L2: Entry 29 of 38 File: USPT Jun 1, 1999

DOCUMENT-IDENTIFIER: US 5908777 A
TITLE: Lipidic vector for nucleic acid delivery

Detailed Description Text (28):
36 .mu.g poly-L-lysine in 400 .mu.L deionized H.sub.2 O was rapidly mixed with 48 .mu.g pRSVluc plasmid DNA, Plautz et al., Proc. Nat'l. Acad. Sci. USA 90: 4645-49 (1993), in 400 .mu.L deionized H.sub.2 O, at DNA/polylysine weight ratio 1:0.75. Aliquots of the resulting DNA/polylysine complex were then rapidly mixed with various amounts of anionic liposomes in equal volumes of deionized H.sub.2 O.

Detailed Description Text (30):
DNA/polylysine (1:0.75) complex became spontaneously encapsulated when rapidly mixed with DOPE/CHEMS (6:4) liposomes. The size of the DNA-containing liposome was dependent on the charge ratio between the DNA/polylysine complex and the anionic liposomes (FIG. 3). When the overall charge was close to neutral, the size of the particles increased over time due to aggregation. A similar charge/size relationship was observed when 0.1 mole % folate-PEG-PE was included in the anionic liposomes during the preparation of folate-targeted liposomes. In order to compare the liposome preparations described above with standard preparations, a cationic liposome DNA/DC-chol complex was prepared according to Gao and Huang, Biochem. Biophys. Res. Comm. 179: 280-85 (1991). Its activity was deemed optimum when prepared at a ratio of 1 .mu.g:10 nM of DNA to liposome.

Previous Doc Next Doc Go to Doc#

L2: Entry 32 of 38 File: USPT Aug 18, 1998

DOCUMENT-IDENTIFIER: US 5795587 A
** See image for Certificate of Correction **
TITLE: Stable lipid-comprising drug delivery complexes and methods for their production

Detailed Description Text (6):
When a drug/lipid/polycation complex having a net positive charge is to be produced, the inclusion of the polycation reduces the amount of lipid which must be mixed with drug to the extent that the positive charge from the lipid may be less than the negative charge from the drug. This reduction in the amount of lipid reduces the toxicity of the polycation-containing formulations. Mole amounts of cationic liposomes to be used in formulating nucleic acid/lipid/polycation complexes may range from about 0.1 nmol to about 200 nmol lipid per 1 .mu.g nucleic acid, more preferably from about 1 to about 25 nmoles lipid per 1 .mu.g nucleic acid depending on the positive charge content of the cationic liposomes. It is to be generally understood that in producing the nucleic acid/lipid and nucleic acid/lipid/polycation complexes of the present invention, the mole amount of liposomes required to produce these complexes will increase as the concentration of nucleic acid mixed with the liposomes is increased.

Detailed Description Text (16):
In a preferred embodiment, the nucleic acid/lipid and nucleic acid/lipid/polycation complexes are produced by slowly adding nucleic acid to the solution of liposome or liposome plus polycation and mixing with a stirring bar where the mixing is allowed to proceed second. Alternatively, the liposome or liposome/polycation mix can be added into a single chamber from a first inlet at the same time the nucleic acid is added to the chamber through a second inlet. The components are then simultaneously mixed by mechanical means in a common chamber.

Detailed Description Text (26):
When a polycation is to be mixed with nucleic acid and cationic liposomes, the polycation may be selected from organic polycations having a molecular weight of between about 300 and about 200,000. These polycations also preferably have a valence of between about 3 and about 1000 at pH 7.0. The polycations may be natural or synthetic amino acids, peptides, proteins, polyamines, carbohydrates and any synthetic cationic polymers. Nonlimiting examples of polycations include polyarginine, polyornithine, protamines and polylysine, polybrene (hexadimethrine bromide), histone, cationic dendrimer, spermine, spermidine and synthetic polypeptides derived from SV40 large T antigen which has excess positive charges and represents a nuclear localization signal. A preferred polycation is poly-L-lysine (PLL). In producing nucleic acid/lipid/polycation complexes of the present invention, the ratio of polycation to nucleic acid is kept fixed while varying the amount of liposome. However, those of skill in the art would recognize that the ratio of polycation to nucleic acid will be affected by the charge density of the liposome to be mixed with the nucleic acid and polycation. For example, if the charge density of liposomes is decreased as a result of changes in the lipid composition of the liposome (eg decreasing the ratio of cationic lipid: neutral lipid in the liposome), the amount of polycation to be mixed with nucleic acid and liposome may be increased to compensate for the decrease in positive charge contributed by the liposomes. However, when polycation is utilized, it is preferred

to use subsaturating amounts of polycation (ie amounts which will not saturate all the negative charge of the nucleic acid) in order to allow the cationic lipids to complex with the nucleic acid. Thus, in a preferred embodiment of the invention, a positive charge excess of lipid to nucleic acid is used even when polycation is mixed with lipid and nucleic acid. Amounts of polycation which may be mixed with 1 .mu.g of nucleic acid and varying amounts of cationic liposomes in the present invention range from about 0.01 .mu.g to about 100 .mu.g of polycation per .mu.g of nucleic acid, preferably from about 0.1 .mu.g to about 10 .mu.g of polycation per .mu.g of nucleic acid.

Detailed Description Text (27):
Where purification of nucleic acid/lipid and nucleic acid/lipid/polycation complexes from excess free DNA, free liposomes and free polycation is desired, purification may be accomplished by centrifugation through a sucrose density gradient or other media which is suitable to form a density gradient. However, it is understood that other methods of purification such as chromatography, filtration, phase partition, precipitation or absorption may also be utilized. In a preferred method, purification via centrifugation through a sucrose density gradient is utilized. The sucrose gradient may range from about 0% sucrose to about 60% sucrose, preferably from about 5% sucrose to about 30% sucrose. The buffer in which the sucrose gradient is made can be any aqueous buffer suitable for storage of the fraction containing the complexes and preferably, a buffer suitable for administration of the complex to cells and tissues. A preferred buffer is pH 7.0-8.0 Hepes.

Previous Doc Next Doc Go to Doc#

First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

Generate Collection Print

L2: Entry 36 of 38 File: USPT Feb 15, 1994

DOCUMENT-IDENTIFIER: US 5286634 A
** See image for Certificate of Correction **
TITLE: Synergistic method for host cell transformation

Brief Summary Text (20):
According to this invention, a recombinant cell can be made comprising nonnative and native DNA in which the nonnative DNA is introduced into the cell by the coordinated use of a polycation compound and a cationic liposome compound during transfection of the cell thereby transforming the cell. Any type of cellular life form can be so transformed although the invention is most efficient when used with a cell lacking a cell wall, that is, a cell having an outer boundary that is a membrane. Types of cells having a membrane as an outer boundary include mammalian cells and protoplasts of either monocotyledonous or dicotyledonous plant cells.

Drawing Description Text (3):
FIG. 2. Autoradiogram of a thin layer chromatography (TLC) plate showing acetylated products of 14C chloramphenicol after transfection of BMS-M with varying DNA concentrations by polycation compound, cationic liposome or 2PC methods. A, unreacted .sup.14 C chloramphenicol; B, 1-acetylchloramphenicol; C, 3-acetyl chloramphenicol. PLCF, also termed 2PC.

Previous Doc Next Doc Go to Doc#

L2: Entry 4 of 38 File: USPT Sep 13, 2005

US-PAT-NO: 6943027
DOCUMENT-IDENTIFIER: US 6943027 B2

TITLE: Preparation of stable formulations of lipid-nucleic acid complexes for efficient in vivo delivery

DATE-ISSUED: September 13, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Papahadjopoulos; Demetrios	San Francisco	CA		
Hong; Keelung	San Francisco	CA		
Zheng; Weiwen	San Francisco	CA		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
The Regents of the University of California	Oakland	CA			02

APPL-NO: 10/121962 [PALM]
DATE FILED: April 12, 2002

PARENT-CASE:
CROSS REFERENCE TO RELATED APPLICATIONS This application is a continuation of U.S. patent application Ser. No. 09/420,908, filed Oct. 20, 1999, now U.S. Pat. No. 6,410,049 which is a continuation of U.S. patent application Ser. No. 08/967,791, filed Nov. 10, 1997, now U.S. Pat. No. 6,071,533, which claims the benefit of the filing date of U.S. Ser. No. 60/030,578, filed Nov. 12, 1996.

INT-CL-ISSUED: [07] C12 N 15/88

US-CL-ISSUED: 435/458; 514/44
US-CL-CURRENT: 435/458; 514/44

FIELD-OF-CLASSIFICATION-SEARCH: 435/458, 514/44
See application file for complete search history.

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
5736392	April 1998	Hawley-Nelson et al.	435/320.1

☐

ART-UNIT: 1636

PRIMARY-EXAMINER: Ketter; James

ATTY-AGENT-FIRM: Townsend and Townsend and Crew LLP

ABSTRACT:

The present invention provides for lipid:nucleic acid complexes that have increased shelf life and high transfection activity in vivo following intravenous injection, and methods of preparing such complexes. The methods generally involve contacting a nucleic acid with an organic polycation to produce a condensed nucleic acid, and then combining the condensed nucleic acid with a lipid comprising an amphiphilic cationic lipid to produce the lipid:nucleic acid complex. This complex can be further stabilized by the addition of a hydrophilic polymer attached to hydrophobic side chains. The complex can also be made specific for specific cells, by incorporating a targeting moiety such as an Fab' fragment attached to a hydrophilic polymer.

25 Claims, 7 Drawing figures

Previous Doc Next Doc Go to Doc#

Hit List

First Hit | Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 6867195 B1

Using default format because multiple data bases are involved.

L3: Entry 1 of 3 File: USPT Mar 15, 2005

US-PAT-NO: 6867195
DOCUMENT-IDENTIFIER: US 6867195 B1

TITLE: Lipid-mediated polynucleotide administration to reduce likelihood of subject's becoming infected

DATE-ISSUED: March 15, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Felgner; Philip L.	Rancho Santa Fe	CA		
Wolff; Jon Asher	Madison	WI		
Rhodes; Gary H.	Leucadia	CA		
Malone; Robert Wallace	Davis	CA		
Carson; Dennis A.	Del Mar	CA		

US-CL-CURRENT: 514/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw

☐ 2. Document ID: US 6436708 B1

L3: Entry 2 of 3 File: USPT Aug 20, 2002

US-PAT-NO: 6436708
DOCUMENT-IDENTIFIER: US 6436708 B1

TITLE: Delivery system for gene therapy to the brain

DATE-ISSUED: August 20, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leone; Paola	Philadelphia	PA	19107	
During; Matthew J.	Philadelphia	PA	19147	
Sorgi; Frank L.	Sonoma	CA	95476	

US-CL-CURRENT: 435/458; 424/450, 435/320.1, 435/455, 514/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

☐ 3. Document ID: US 5891689 A

L3: Entry 3 of 3 File: USPT Apr 6, 1999

US-PAT-NO: 5891689
DOCUMENT-IDENTIFIER: US 5891689 A

TITLE: Heme-bearing microparticles for targeted delivery of drugs

DATE-ISSUED: April 6, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Takle; Garry B.	New York	NY		
George; Shaji T.	New York	NY		

US-CL-CURRENT: 435/458; 424/450, 435/174, 435/456, 514/44

Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | KWIC | Draw D

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Terms	Documents
L1 and (multivesicular)	3

Display Format: - Change Format

Previous Page Next Page Go to Doc#